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Cardiac wasting is not cardiac cachexia: the problem of the subjective/objective genitive in matters of the heart

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Tessitore, Costelli *et al*. were among the first to report a previously unnoticed loss of heart mass in cachectic mice suffering from a severe tumor burden.[1] At the time both the general consensus definition of cachexia[2] and the cancer cachexia classification[3] did not exist. In particular, cancer cachexia is a syndrome characterized by muscle wasting leading to body weight loss in the presence of cancer.[3-5] More recently, Zhou *et al*. highlighted once more the existence of a tumor-induced loss of heart mass in a murine model of cancer cachexia.[6] This study generated a new line of research aimed at exploring the mechanisms underlying cardiac wasting in the presence of cancer. Cardiac wasting in the presence of cancer-induced cachexia is distinct from and other than cardiac cachexia, *i.e.* the atrophy of skeletal muscle induced by cardiac pathologies.[7] To add insult to injury, some authors use the expression "muscle cachexia" meaning muscle atrophy,[8] which, as a consequence, may suggest to naive readers that cardiac cachexia is a form of cardiac muscle atrophy. We aim here to clarify the terminology describing these conditions, so as to avoid the misleading use of related expressions: cardiac atrophy and cardiac cachexia may sound alike but are very different. In particular, it is the expression "cardiac cachexia" that raises a problem of ambiguity and should be handled with care.

The age-old problem of the subjective/objective genitive case

Does the Latin expression *timor barbarorum* – literally, the fear of barbarians – mean the fear the ancient Romans had of barbarians or the one barbarians had of Romans? Only the context helps one to distinguish between the two options, since the genitive case in Latin can express either. Albeit English differentiates the two options through syntax - with the Saxon genitive or through the order of words - disambiguation remains difficult sometimes. To use a dramatically contemporary example in English, what does "foreigner hating" mean? The fact that we hate foreigners or that foreigners hate us?

Due to the use of the expression "muscle cachexia" introduced by some authors to wrongly denote muscle atrophy - 66 papers in PubMed – the compound "cardiac cachexia" may also give rise to the problem of the subjective/objective genitive: does it mean cachexia induced by cardiac problems or atrophy of the cardiac muscle induced by cachexia? Unquestioningly not the latter. The use of "cardiac cachexia" to indicate cardiac atrophy is incorrect.

What, then, is cardiac cachexia?

More than 400 papers to date refer to cardiac cachexia as a syndrome of skeletal muscle wasting associated to a specific pathology, *i.e.* Chronic Heart Failure (CHF). Indeed, cardiac cachexia refers to the fact that skeletal muscle, and not cardiac muscle, is dismantled in CHF-induced cachexia. Following the discovery that cardiac wasting also exists in cachexia,[6] it appears that the heart can be both the trigger and the target of cachexia. We are concerned that the use of the expression "cardiac cachexia" may be mistakenly used in both its subjective and objective senses.

Different options to indicate cardiac wasting: PROs and CONs

As stated above, cardiac muscle wasting is not cardiac cachexia. The following are alternative ways to refer to the phenomenon of cardiac wasting: i) atrophy of the heart: this

expression is unambiguous, even though relatively long; it is very general and requires the need to clarify the context in which the atrophy arises, e.g. cancer-induced atrophy of the heart to specify that the trigger is cancer; ii) heart atrophy, which is synonymous with atrophy of the heart and is equally generic; iii) cardiac atrophy, which means atrophy of the heart but sounds dangerously similar to cardiac cachexia; iv) cachectic heart, a more holistic expression not often used to date; v) cardiac wasting, which suggests a pathological condition and is a specific, easily discernible expression, being, therefore, our favorite.

Highlighting cardiac wasting in the definition of cachexia

The current consensus definition of cachexia[2] does not explicitly refer to the loss of cardiac muscle. We think it is appropriate to bear well in mind that both skeletal and cardiac musculature are involved when reporting muscle wasting in cachexia. Cardiac wasting in cachexia leads to heart dysfunction, which ultimately increases the risk of death of cachectic patients due to cardiovascular complications.

List of abbreviations

CHF, Chronic Heart Failure

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